IN THE CLAIMS:

1. (original) A null mutant rodent comprising in its germ cells an artificially induced PTTG null mutation.

2. (original) The null mutant rodent of claim 1, wherein functional PTTG protein is not expressed in the somatic cells of said rodent.

3. (original) The null mutant rodent of claim 1, wherein the cells of said rodent lack the ability to endogenously express functional PTTG protein.

4. (original) The null mutant rodent of claim 1, wherein both PTTG genes have been artificially mutated by way of homologous recombination.

5. (original) The null mutant rodent of claim 1, wherein the PTTG null mutant was generated by a mating of a male rodent and female rodent of the same species each bearing at least one artificially mutated PTTG allele.

6. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of homologous recombination.

7. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in an embryonic stem cell.

8. (presently amended) The null mutant rodent of claim 7, wherein the embryonic stem cell is from the stem cell line ~~is~~ murine ES J-1.

9. (original) The null mutant rodent of claim 7, wherein said embryonic stem cell is injected into a blastocyst, and wherein the blastocyst is implanted into a pseudopregnant rodent.

10. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in an embryonic stem cell, and wherein at least one rodent genomic copy of the PTTG gene in the embryonic stem cell recombines with a targeting vector containing a selectable genetic marker sequence, such that said targeting vector is inserted into the genome of said embryonic stem cell.

11. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele contains a deletion of the translation start site.

12. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele contains a deletion of the KOZAK region.

13. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele contains a deletion of a segment of the endogenous PTTG gene promoter region.

14. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele contains a deletion of the transcription start codon.

15. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of site specific recombination.

16. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of transpositional recombination.

17. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of a frame shift mutation.

18. (original) The null mutant rodent of claim 5, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in a germ cell.

19. (original) The null mutant rodent of claim 18, wherein the germ cell is an oocyte.

20. (original) The null mutant rodent of claim 18, wherein the germ cell is a male germ cell.

Claims 21-24 (cancelled)

25. (original) The null mutant rodent of claim 1, wherein the rodent is a mouse.

26. (original) The null mutant rodent of claim 1, wherein the rodent is a rat.

27. (original) A null mutant rodent comprising in its germ cells an artificially induced PTTG null mutation, wherein said mutation results in said rodent exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a rodent lacking said mutation.

28. (original) A rodent whose germ line comprises an artificially induced PTTG null mutation, wherein both mutated PTTG genes are transmitted to said rodent by a mating of a male rodent and female rodent of the same species each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG KOZAK sequence from which the KOZAK sequence has been deleted and replaced with polynucleotides exogenous to the PTTG gene, and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous KOZAK sequence.

29. (original) A rodent whose germ line comprises an artificially induced PTTG null mutation, wherein both mutated PTTG genes are transmitted to said rodent by a mating of a male rodent and female rodent of the same species each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG translation start site from which the translation start site has been deleted and replaced with polynucleotides exogenous to the PTTG gene; and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous translation start site.

30. (original) A rodent whose germ line comprises an artificially induced PTTG null mutation, wherein both mutated PTTG genes are transmitted to said rodent by a mating of a male rodent and female rodent of the same species each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG transcription start codon from which the transcription start site has been deleted and replaced with polynucleotides exogenous to the PTTG gene; and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous transcription start codon.

Claims 31-35 (cancelled)

36. (currently amended) An animal model for diabetes comprising a ~~the~~ null mutant rodent ~~of any of claims 1, 27-30~~ comprising in its germ cells an artificially induced PTTG null mutation.

37. (new) A method for studying mammalian physiology at the cellular level, tissue level, organismal level or any combination thereof, comprising:

providing a null mutant rodent comprising in its germ cells an artificially induced PTTG null mutation; and

using the null mutant rodent in the study of mammalian physiology.

38. (new) The method of claim 37, wherein using the null mutant rodent in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of diabetes, hyperglycemia, hypoinsulinaemia, and hypoleptinemia.

39. (new) The method of claim 37, wherein using the null mutant rodent in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of chromosomal aneuploidy, premature centromere division, chromosomal damage, the mitotic cellular pathway, and cell cycle control.

40. (new) The method of claim 37, wherein using the null mutant rodent in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of thrombocytopenia, thymic hyperplasia, and splenic hypoplasia.

41. (new) The method of claim 37, wherein using the null mutant rodent in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of testicular hypoplasia and female subfertility.

42. (new) A null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation.

43. (new) The null mutant mouse of claim 42, wherein functional PTTG protein is not expressed in the somatic cells of said mouse.

44. (new) The null mutant mouse of claim 42, wherein the cells of said mouse lack the ability to endogenously express functional PTTG protein.

45. (new) The null mutant mouse of claim 42, wherein both PTTG genes have been artificially mutated by way of homologous recombination.

46. (new) The null mutant mouse of claim 42, wherein the PTTG null mutant was generated by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele.

47. (new) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of homologous recombination.

48. (new) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in an embryonic stem cell.

49. (new) The null mutant mouse of claim 48, wherein the embryonic stem cell is from the stem cell line murine ES J-1.

50. (new) The null mutant mouse of claim 48, wherein said embryonic stem cell is injected into a blastocyst, and wherein the blastocyst is implanted into a pseudopregnant mouse.

51. (new) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of homologous recombination in an embryonic stem cell, and wherein at least one mouse genomic copy of the PTTG gene in the embryonic stem cell recombines with a targeting vector containing a selectable genetic marker sequence, such that said targeting vector is inserted into the genome of said embryonic stem cell.

52. (new) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele contains a deletion of the translation start site, the KOZAK region, a segment of the endogenous PTTG gene promoter region, the transcription start codon, or any

combination thereof.

53. (new) The null mutant mouse of claim 46, wherein said at least one mutated PTTG allele is generated by way of site specific recombination, transportational recombination, a frame shift mutation, homologous recombination in a germ cell, or any combination thereof.

54. (new) The null mutant mouse of claim 53, wherein the germ cell is an oocyte or a male germ cell.

55. (new) A null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation, wherein said mutation results in said mouse exhibiting at least one phenotype selected from the group consisting of hyperglycemia, hypoinsulinaemia, hypoleptinemia, diabetes, chromosomal aneuploidy, premature centromere division, chromosomal damage, aberrant mitotic cellular division, thrombocytopenia, thymic hyperplasia, splenic hypoplasia, testicular hypoplasia, and female subfertility, the prevalence of which is greater than in a mouse lacking said mutation.

56. (new) A mouse whose germ line comprises an artificially induced PTTG null mutation, wherein both mutated PTTG genes are transmitted to said mouse by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG KOZAK sequence from which the KOZAK sequence has been deleted and replaced with polynucleotides exogenous to the PTTG gene, and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous KOZAK sequence.

57. (new) A mouse whose germ line comprises an artificially induced PTTG null mutation, wherein both mutated PTTG genes are transmitted to said mouse by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG translation start site from which the translation start site has been deleted and replaced with polynucleotides exogenous to the PTTG gene; and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous translation start site.

58. (new) A mouse whose germ line comprises an artificially induced PTTG null mutation, wherein both mutated PTTG genes are transmitted to said mouse by a mating of a male mouse and female mouse each bearing at least one artificially mutated PTTG allele; said at least one mutated PTTG allele is generated by way of homologous recombination with a targeting vector; and said targeting vector further comprises a selectable genetic marker; said targeting vector contains a polynucleotide sequence comprising a segment of PTTG genomic DNA or a PTTG cDNA spanning the PTTG transcription start codon from which the transcription start site has been deleted and replaced with polynucleotides exogenous to the PTTG gene; and said exogenous polynucleotides are flanked by at least about 200 polynucleotide base pairs that are complementary to polynucleotide regions of an endogenous PTTG gene which flank the endogenous transcription start codon.

59. (new) An animal model for diabetes comprising a null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation.

60. (new) A method for studying mammalian physiology at the cellular level, tissue level, organismal level or any combination thereof, comprising:

providing a null mutant mouse comprising in its germ cells an artificially induced PTTG null mutation; and

using the null mutant mouse in the study of mammalian physiology.

61. (new) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of diabetes, hyperglycemia, hypoinsulinaemia, and hypoleptinemia.

62. (new) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of chromosomal aneuploidy, premature centromere division, chromosomal damage, the mitotic cellular pathway, and cell cycle control.

63. (new) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of thrombocytopenia, thymic hyperplasia, and splenic hypoplasia.

64. (new) The method of claim 60, wherein using the null mutant mouse in the study of mammalian physiology further includes examining a role of PTTG in connection with regulation of a physiological phenomenon selected from the group consisting of testicular hypoplasia and female subfertility.